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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,306	10/17/2000	Ian Reginald Reid	11752-002001	7673

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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,306	REID ET AL.	
	Examin r	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3-23-00, 9-4-02 and 10-2-03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *12-33,38-40 and 42-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,34-37 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

Claims 1-51 are pending.

Applicants' preliminary amendment filed 23 March 2000, which amends claims 4-5, 9-10, 15-16 and 20-22, applicants' amendment filed 4 September 2002, which amends claims 11, 22, 30, 33, 37 and 40, and Applicants' request (filed 2 October 2003) for extension of time of one month have been entered.

Foreign priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119 (a)-(d) based on an application filed in New Zealand on 26 September 1999.

Election/Restrictions

Applicant's election (see the response filed 2 October 2003) of Group I, claims 1-11, 34-37 and 41 without traverse are acknowledged. Claims 12-33, 38-40 and 42-51 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected inventions. It is noted that a clear and obvious typographical error occurred in the restriction wherein claims 12-18 which read on a method of Group II using adrenomedullin NOT amylin were improperly included in Group II which are drawn to a method using amylin. Therefore, claims 12-18 are drawn to nonelected inventions.

Thus, elected claims 1-11, 34-37 and 41 are under examination to the extent that they are drawn to the elected invention.

Specification Objections

The disclosure is objected to because of the following informalities:

The specification does not comply with one or more parts of 37 CFR 1.821-1.825. See page 1, beginning at line 15, where amylin peptide sequence is recited without the requisite "SEQ ID NO:"

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claim 41 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, the second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-11, 34-37 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 recite "the active concentration"; the recitation is indefinite because the specification does not define what the effective concentration is. Also, claims 1-3 lack antecedent basis for the limitation "the active concentration because claims 1-3 are the first recited independent claims. The dependent claims are also rejected.

Claim 6 recites "or analog thereof"; the recitation is unclear as to whether or not the generic term "analog" includes amylin antagonist. Given included, how would the claimed method be operative using the antagonist? Note that the specification does not expressly define analog in this regard. See also claims 7-8, 10, 34, 36 and 41. The dependent claims are also rejected.

Claim 34 recites "... which is effective in inducing chondrocyte proliferation"; the recitation is unclear as to what subject is effective. Is the claimed *method,* or, the recited *amount* of amylin effective in inducing chondrocyte proliferation ?

Claim 41 provides for the use of amylin or an analog thereof; but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/ process applicant is intending to encompass. Also, claim 41 is unclear where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claim 41 is a non-statuary claim which recites a "use"; " a use" is not a statutory claim of invention. Further, claim 41 is indefinite in the recitation "effecting chondrocyte proliferation"; what is consequence of effecting chondrocyte proliferation, stimulation or suppression?

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-10, 34-36 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a method of treating a patient to stimulate bone growth or chondrocyte proliferation or cartilage growth comprising administering to the patient amylin *per se* or amylin-(1-8) as described in pages 10-11 and 13. Applicant is not in possession of a method of treating the same comprising administering to the patient amylin analog (see claims 6-10, 34-36 and 41).

The claims are broadly drawn to a method of facilitating bone or cartilage growth comprising administering to a subject amylin *analog* or amylin mutant or derivative (e.g., insertion a heterologous polypeptide that is structurally irrelevant to amylin *per se*). There is insufficient guidance and direction as to make and use amylin analogs, wherein the analogs are products generated by insertion, deletion or substitution (see page 6, paragraph four). The specification is silent in characterization of amylin analogs (variants) having comparable activity of unmodified amylin molecule.

The specification defines the amylin analog as a protein which is a variant molecule generated by insertion, deletion or substitution of amino acid residues (see page 6, paragraph four). The specification does not teach or provide guidance as to how to make and characterize positive variants that retain the desired amylin activity from a "mutant pool". The specification

provides no factual evidence for identifying and characterizing the *core* sequence which is critical for the bioactivity of the variants. The claimed analog is based upon a theoretical assumption (i.e., contemplation, see page 6, line 19) rather than actual reduction to practice. Thus, the amylin analog is insufficiently described in the current application. The activity of the analog thereof is highly unpredictable after mutational alteration to the amylin structure –insertion, deletion or/and substitution.

The specification has described use of rat amylin and amylin-(1-8) peptide (see pages 11-12). However, the specification is silent in teaching biological activity of insertion and substitution mutants of amylin, or/and pharmacological efficacy of the mutants in conjunction with cyto-toxicity. It has been shown that amylin variant (substitution mutant) has unpredictable toxicity toward subject administered with the variant peptide (see Ng, M. C. Y. et al., *Diab. Care* (2001) 24, 663-671); such the variant does not have the biological properties representative of what is being claimed (e.g., amylin-(1-8). Thus, without guidance or a representative working example specially regarding substitution or/and insertion mutation of amylin in light of pharmacological potency and cyto-toxicity of the mutant, use of the amylin analogs or mutants is highly unpredictable.

In addition, the amylin analog could be amylin antagonist because the specification does not define whether the generic analog encompasses only agonist, or only antagonist, or both agonist and antagonist. Such the antagonist has a pharmacological function not disclosed in the current disclosure. Thus, applicant is deemed not in possession of the claimed method comprising use of the amylin analog.

Protein higher structures, e.g., secondary and ternary structure, are considered critical for protein function. Without exception, it has been demonstrated that reduced amylin-(1—8) (cleavage of an intermolecular the disulfide bond between residues 2 and 7) has no agonist effect but acts as an antagonist to the effects of either amylin or amylin-(1—8) that possesses the disulfide bond thereof (see Cornish, J. (1998) *Am. J. Physiol. Endocrinol. Metab.* 274: E827-E833). Thus, insurance of formation correct disulfide linkage contributes to maintain biological activity of amylin analog, and to successful use of the produced amylin in the claimed method. Yet, the specification provides no guidance or teaching in this regard, i.e., how to produce, identify and characterize functional mutants. The current disclosure does not enable claimed method that requires functional amylin analog (mutant) for treating the patient in need for stimulating bone or cartilage development. Thus, applicants are not in possession of the claimed method.

Applicant has disclosed only a method of facilitating bone or cartilage growth comprising administering to the patient amylin polypeptide (37 amino acids) and amylin-(1-8) peptide (8 amino acid); therefore, the skilled artisan cannot envision all the contemplated peptide sequence possibilities recited in the instant claims as analog is a broad language encompassing a large number of mutants (see the above statement). Consequently, conception cannot be achieved until sufficient description of core structure attributed to the amylin substantial activity and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993).

Description of invention's reduction to practice, unaccompanied by any meaningful, distinguishing characteristics of evolved the polypeptide variants or derivatives and their use as chondrocyte-proliferating composition is insufficient to satisfy written description requirement of 35 U.S.C. §112, since, in context of present case, disclosure of manner in which invention was reduced to practice does not satisfy more fundamental written description requirement set forth in Section 112.

One of skill in the art would reasonably conclude that the disclosure fails to sufficiently describe amylin analogs and thus does not support enablement for the claimed methods using the amylin analog thereof. Therefore, Applicant was not in possession of the claimed amylin analog or derivative.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 8-10, 34-36, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Reid, I. R. et al. (WO 9602269).

Reid et al. teach a method of treating a patient in need of stimulating bone growth comprising administering amylin or amylin agonist to the patient (see the patent claims 1 and 6-7 and pages 2-3), as applied to claims 8-10 of the current application.

Also, Reid et al. teach use of amylin in the preparation of a medicament for stimulating bone growth, as applied to the application claim 41.

Note that the above-mentioned claims are anticipated by the Reid et al. teachings because Reid et al. method for stimulating bone growth comprises the same step, i.e., administering amylin to the patient wherein administration of amylin to the patient inevitably lead to augmenting chondrocyte proliferation since the consequence of the administration, i.e., stimulating bone growth and chondrocyte proliferation (a part of bone growth) is inherent in the step of the claimed method; the same method comprising the same composition and steps must result in the identical endpoint. Therefore, the application claims 1-7 and 34-36 are anticipated by the Reid et al. teaching as well.

Claim Rejection –Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

Claims 8 and 9 are rejected under the judicially created doctrine of the obviousness-type double patenting of the claims 4-11 in US Pat. No. 5922677. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 4-11 of Patent 5922677 disclose a method of stimulating bone growth comprising administering to a patient amylin (see column 4, lines 19-23), which is an obvious variation of the application claims 8-9.

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel W. Liu, Ph.D.

November 25, 2003

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER